**REMARKS**

**Rejections under 35 U.S.C. §112, first paragraph**

The Examiner again rejects claims 1, 2, 4-6, 8, 9, 16 and 24-25 as lacking enablement for R1 and R2 being all mono- or polycyclic groups, mono or poly heterocyclic groups, aralkyl groups and heteroalkyl groups. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

1) *Claim 15* - The Examiner included claim 15 in the rejection; however Applicants believe this to be in error. Claim 15 has only been objected to on the transmittal of the Office Action and claim 15 is further drawn to specific compounds. Clarification of this issue is respectfully requested.

2) *Claims 1, 2, 4, 6, 8, 9, 16 and 24-25* - The Examiner maintains the rejection of these claims for lack of enablement. Pages 3 and 4 simply repeat the previously issued rejection. On page 4, final paragraph through page 6, first paragraph of the Office Action, the Examiner offers her "rebuttal" to Applicants' arguments of February 13, 2002. However, while the Examiner has now recited the factors that the Federal Circuit set forth in *In re Wands* for determining enablement, she has still failed provide a proper analysis. The only analysis that the Examiner has arguably

made is with regard to the first factor, i.e. that the breathe of the claims may be considered large. With regard to any of the other Wand's factors, the Examiner has only made conclusory and unsupported statements. For example, the Examiner states on page 5,

> In terms of the fifth Wands factor, the specification discloses that all of the test compounds showed activity at a final concentration of about 10 microMoles, and that these compounds are therefore are SK/IK/BK channel modulating agents. However, the specification does not go into how effective these compounds are in modulating these channels.

The above statements are not a proper application of the fifth Wands factor. The Examiner has failed to provide any scientific basis for why Applicants would need to, in the specification, "go into how effective these compounds are in modulating these channels." Similarly, the Examiner on page 6 has failed to provide any evidence of lack of predictability in the field of the invention or why the tests in the specification are insufficient to support the enablement of the recited Markush group. It is similarly improper to issue the conclusory statement that the claimed invention "would require undue experimentation" without supporting the statement with pertinent scientific evidence or reasoning.

Applicants note that the holding of In re Marzocchi and Horton, 169 USPQ 367 (CCPA 1971), was in no way overturned or modified by the court in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988), and thus remains precedential law. Under the holding of In re Marzocchi, a claimed invention is presumed to be enabled and the burden is on the Examiner to provide evidence for a rejection of lack of enablement. As noted previously, the Court of Customs and Patent Appeals very clearly directed in In re Marzocchi that

> It is incumbent upon the Patent Office, whenever a rejection on this basis [,lack of enablement,] is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own **with acceptable evidence or reasoning** which is inconsistent with the contested statement. In re Marzocchi and Horton, 169 USPQ 367 (CCPA 1971 *(emphasis added)*

Applicants request that the Examiner either support the rejection with acceptable evidence or reasoning or withdraw the rejection.

**Rejections under 35 U.S.C. §112, second paragraph**

The Examiner maintains the rejection of claims 1, 2, 4-6, 8, 9 and 16 under 35 U.S.C. §112, second paragraph as being indefinite. Specifically, the Examiner maintains that the terms mono- or polycyclic groups, mono or poly heterocyclic groups, aralkyl groups and heteroalkyl are indefinite. However, the Examiner has failed

to address Applicants' arguments of February 13, 2002, which is procedurally improper. The Examiner's attention is directed to M.P.E.P. §707.07(f) "Answer All Material Traversed," which instructs Examiners that

> Where the applicant traverses any rejection, the examiner should, if he or she repeats the rejection, take note of the applicant's argument **and answer the substance of it**. *(emphasis added)*

Applicants' response of February 13, 2002 traversed the rejection of the claims as being unclear under 35 U.S.C. §112, second paragraph. Applicants further submitted both arguments and evidence in support of their position. The Examiner has failed to in any way address Applicants' evidence and arguments and has simply verbatim repeated the rejection. This action by the Examiner is procedurally improper and prejudicial against the patent term, for any patent issuing from the application. The Examiner is requested to properly consider all arguments, evidence and amendments made previously or herein and to either substantively rebut the submission by Applicants or withdraw the rejection.

To facilitate the prosecution of the application, Applicants have further amended the claims to further define mono- or

polycyclic groups, mono or poly heterocyclic groups, aralalkyl groups and hetero-alkyl groups as follow.

> an unsaturated or a partially or completely saturated mono- or polycyclic **aromatic hydrocarbon** group, a mono or poly heterocyclic group **containing one or more 5- and/or 6-membered cyclic groups having one or more heteroatoms selected from the group consisting of N, O and S; an aryl group attached to an alkyl group;** or a hetero-alkyl **having an alkyl group attached to a mono or poly heterocyclic group containing one or more 5- and/or 6-membered cyclic groups having one or more heteroatoms selected from the group consisting of N, O and S**

As all terms in the claims are adequately and clearly defined, withdrawal of the rejection is respectfully requested.

The Examiner rejects claim 21 on the basis that there is no recitation in the claim of "an effective" amount of the compound being administered to a patient in need thereof. Applicants traverse this rejection and withdrawal thereof is respectfully requested. The Examiner is incorrect in this rejection because claim 21 is drawn to a composition, not a method of treatment. As such, it would be improper to recite an active step, such as administering the composition to a patient. Withdrawal of the rejection is respectfully requested.

The Examiner further rejects claim 1 as being indefinite in the recitation of "may optionally be." Claim 1 has been amended to recite:

> ~~which~~ **wherein said** mono- or polycyclic groups or aralkyl or hetero-alkyl groups **are unsubstituted or are substituted** ~~may optionally be substituted~~ one or more times with substituents selected from the group consisting of....

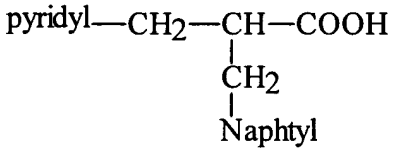
Withdrawal of the rejection is respectfully requested.

**Rejections under 35 U.S.C. §102(b)**

The Examiner maintains the rejection of claims 1, 2, 4-6, 8 and 16 have been rejected under 35 U.S.C. §102(b) as being anticipated by Morisawa et al. Morisawa et al. is asserted to teach propanedioic acid (4-fluorophenyl)(3-pyridinylmethyl)-diethyl ether, which is encompassed by the present claims. In the rejection the Examiner again cites the entire 111-page document of Morisawa et al., without specifically pointing out where the Examiner believes that present invention is disclosed in the reference. In a telephone interview with Applicants' representative the Examiner clarified that she was relying on the disclosure of the compound of Preparation 3 on page 90 of the

reference, i.e. the compound 2(RS)-(1-Naphthyl)methyl-3-(3-pyridyl)propionic acid, as falling within the scope of claim 1.

Applicants traverse this rejection and withdrawal thereof is respectfully requested. The compound 2(RS)-(1-Naphthyl)methyl-3-(3-pyridyl)propionic acid, which is asserted by the Examiner to fall within the scope of the present claims has the following structure.




The central carbon of 2(RS)-(1-Naphthyl)methyl-3-(3-pyridyl)propionic acid of Moriwasa et al. is linked to a hydrogen group. However, as seen from formula I of the present claim 1, none of the four groups of the compounds of the invention, $R^1A$, $R^2F$, $R^3$ or $R^4$ can be hydrogen. Thus, 2(RS)-(1-Naphthyl)methyl-3-(3-pyridyl)propionic acid of Moriwasa et al. falls outside of the scope of the present invention. As Moriwasa et al. fails to disclose the present invention, withdrawal of the rejection is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully

requested to contact MaryAnne Armstrong, PhD (Reg. No. 40,069) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

**Attached hereto is a marked-up version of the changes made to the application by this Amendment.**

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of three (3) months to October 24, 2002 in which to file a reply to the Office Action. The required fee of $920.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees

required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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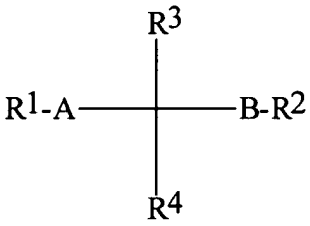
Attachment: Version with Markings to Show Changes Made

(Rev. 09/26/01)

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE CLAIMS:**

1. (Amended) A chemical represented by the general formula I




(I)

and a pharmaceutically acceptable salt or an oxide or a hydrate thereof, wherein,

A and B, independently of each another represent a group of the formula -CH2)n-, of the formula -(CH2)n-Y- (in either direction), or of the formula -(CH2)n-Y-(CH2)m;

in which formulas

n and m, independently of each other, represent 0, 1, 2, 3 or 4, and Y represents O, S, or NR''', wherein R''' represents hydrogen or alkyl;

R1 and R2, independently of each other, represent

alkyl, alkenyl, alkynyl, cycloalkyl, amino, trihalogenmethyl, nitro, cyano, or phenyl, or a group of the formula -OR', -SR', -R'OR", -R'SR", -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', -C(O)NR'(OR"), -C(S)NR'(OR"), -C(O)NR'(SR"),

-C(S)NR'(SR"), -CH(CN)2, -C(O)NR'R", -C(S)NR'R", -CH[C(O)R']2, -CH[C(S)R']2, -CH[C(O)OR']2, -CH[C(S)OR']2, -CH[C(O)SR']2, -CH[C(S)SR']2, CH2OR', CH2SR', -NR'C(O)R", or -OC(O)R';

an unsaturated or a partially or completely saturated mono- or polycyclic aromatic hydrocarbon group, a mono- or poly-heterocyclic group containing one or more 5- and/or 6-membered cyclic groups having one or more heteroatoms selected from the group consisting of N, O and S; [an aralkyl group,] an aryl group attached to an alkyl group; or a hetero-alkyl group having an alkyl group attached to a mono or poly heterocyclic group containing one or more 5- and/or 6-membered cyclic groups having one or more heteroatoms selected from the group consisting of N, O and S, [which] wherein said mono- or polycyclic groups or aralkyl or hetero-alkyl groups are unsubstituted or are substituted [may optionally be substituted] one or more times with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, alkenyl, alkynyl, amino, nitro, cyano, or amido, or a group of the formula -R', -OR', -SR', -R'OR", -R'SR", -C(O)R', -C(S)R', -C(S)OR', -C(S)OR', -C(O)SR', or -C(S)SR', or a phenyl or a phenoxy group, [which] wherein said phenyl or phenoxy groups [may optionally be substituted on] are unsubstituted or substituted one or more times

with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, alkenyl, alkynyl, amino, nitro, cyano, or amido, or a group of the formula -R', -OR', -SR', -R'OR", -R'SR", -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', -NR'C(O)R", or -OC(O)R';

wherein

R' and R", independently of each another, represent hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy or phenyl, or a group of the formula NR"'R"", wherein R"' and R"", independently of each another, represent hydrogen or alkyl;

R3 and R4, independently of each another, represent

alkyl, alkenyl, alkynyl, cycloalkyl, amino, trihalogenmethyl, nitro, cyano, or phenyl, or a group of the formula -OR', -SR', -R'OR", -R'SR", -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', -C(O)NR'(OR"), -C(S)NR'(OR"), -C(O)NR'(SR"), -C(S)NR'(SR"), -CH(CN)2, -C(O)NR'R", -C(S)NR'R", -CH[C(O)R']2, -CH[C(S)R']2, -CH[C(O)OR']2, -CH[C(S)OR']2, -CH[C(O)SR']2, -CH[C(S)SR']2, CH2OR', CH2SR', -NR'C(O)R", or -OC(O)R';

wherein

R' and R", independently of each another, represent hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy or phenyl, or a group

of the formula NR"'R"", wherein R"' and R"", independently of each another, represent hydrogen or alkyl;

or R3 and R4 together form an unsaturated or a partially or completely saturated mono- or polycyclic aromatic hydrocarbon group, or a mono- or poly-heterocyclic group, [which] containing containing one or more 5- and/or 6-membered cyclic groups having one or more heteroatoms selected from the group consisting of N, O and S; wherein said mono- or polycyclic groups [may optionally be] are unsubstituted or substituted one or more times with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, alkenyl, alkynyl, amino, nitro, cyano, or amido, or a group of the formula -R', -OR', -SR', -R'OR", -R'SR", -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', or -C(S)SR', or a phenyl or a phenoxy group, [which] wherein said phenyl or phenoxy groups [may optionally be substituted on] are unsubstituted or substituted one or more times with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, alkenyl, alkynyl, amino, nitro, cyano, or amido, or a group of the formula -R', -OR', -SR', -R'OR", -R'SR", -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', -NR'C(O)R", [or] and -OC(O)R';

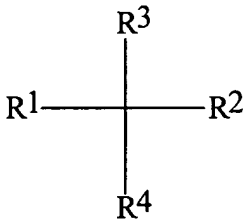
wherein

R' and R", independently of each another, represent hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy or phenyl, or a group of the formula NR"'R"", wherein R"' and R"", independently of each another, represent hydrogen or alkyl.

6. (Amended) The chemical compound according to any of claims 1-5, wherein R1 and R2 independently of each another represents a hydroxy group; an alkyl group; an alkoxy group; a group of the formula -OC(O)R' wherein R' is hydrogen or alkyl; a group of the formula -NHC(O)R", wherein R" is hydrogen or alkyl; a phenyl or a benzyl group, [which] wherein said phenyl and benzyl groups [may optionally be] are unsubstituted or substituted one or more times with substituent selected from the group consisting of alkyl, alkoxy, halogen, CF3, CN, amino, nitro, or a group of the formula -NHC(O)R", wherein R" is hydrogen, alkyl or phenyl; a 5- or 6-membered mono- or poly-heterocyclic group, [which] wherein said heterocyclic group [may optionally be] is unsubstituted or substituted one or more times with substituent selected from the group consisting of halogen, CF3, CN, amino or nitro; a heteroalkyl group, wherein the heterocyclic a mono-heterocyclic group, [which] wherein said heterocyclic group [may optinally be] is unsubstituted or

substituted one or more times with substituent selected from the group consisting of halogen, CF3, CN, amino or nitro.

16. (Amended) The chemical compound according to claim 1, represented by the general formula VI




(VI)

and a pharmaceutically acceptable salt or an oxide or a hydrate thereof,

wherein,

R1 and R2, independently of each other, represent an unsaturated or a partially or completely saturated mono- or polycyclic aromatic hydrocarbon group, a mono- or poly-heterocyclic group, [an aralkyl group] containing one or more 5- and/or 6-membered cyclic groups having one or more heteroatoms selected from the group consisting of N, O and S, an aryl group attached to an alkyl group, or a hetero-alkyl group having an alkyl group attached to a mono- or poly-heterocyclic group containing one or more 5- and/or 6-membered cyclic groups having one or more

heteroatoms selected from the group consisting of N, O an S, [which] wherein said mono- or polycyclic groups or aralkyl or hetero-alkyl groups [may optionally be] are unsubstitued or substituted one or more times with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, alkenyl, alkynyl, amino, nitro, cyano, or amido, or a group of the formula -R', -OR', -SR', -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', or OC(S)SR', or a phenyl or a phenoxy group, [which] wherein said phenyl or phenoxy groups [may optionally be substituted on] are unsubstituted or substituted or more times with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, alkenyl, alkynyl, amino, nitro, cyano, or amido, or a group of the formula -R', -OR', -SR', -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', -NR'C(O)R', or -OC(O)R';

wherein

R' represents hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy or phenyl, or a group of the formula NR"'R"", wherein R"' and R"', independently of each another, represent hydrogen or alkyl; and

R3 and R4, independently of each another, represent

alkyl, alkenyl, alkynyl, cycloalkyl, amino, trihalogenmethyl, nitro, cyano, or phenyl, or a group of the formula -OR', -SR', -R'OR", -R'SR", -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', -C(O)NR'(OR"), -C(S)NR'(OR"), -C(O)NR'(SR"), -C(S)NR'(SR"), -CH(CN)2, -C(O)NR'R", -C(S)NR'R", -CH[C(O)R']2, -CH[C(S)R']2, -CH[C(O)OR')2, -CH[C(S)OR']2, -CH[C(O)SR']2, -CH[C(S)SR']2, CH2OR', CH2SR', -NR'C(O)R", or -OC(O)R';

wherein

R' and R", independently of each another, represent hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy or phenyl, or a group of the formula NR"'R"", wherein R"' and R"", independently of each another, represent hydrogen or alkyl;

or R3 and R4 together form an unsaturated or a partially or completely saturated mono-or polycyclic aromatic hydrocarbon group, or a mono-or poly-heterocyclic group containing one or more 5- and/or 6-membered cyclic groups having one or more heteroatoms selected from the group consisting of N, O and S, [which] mono- or polycyclic groups [may optionally be] are unsubstituted or substituted one or more times with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, alkenyl, alkynyl, amino, nitro, cyano, or amido, or a

group of the formula -R', -OR', -SR', -R'OR", -R'SR", -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', or -C(S)SR', or a phenyl or a phenoxy group, [which] wherein said phenyl or phenoxy groups [may optionally be substituted on] are unsubstituted or substituted one or more times with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, alkenyl, alkynyl, amino, nitro, cyano, or amido, or a group of the formula -R', -OR', -SR', -R'OR", -R'SR", -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', [or] and -C(S)SR';

wherein

R' and R", independently of each another, represent hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl or alkoxy, or a group of the formula NR"'R"", wherein R"' and R"", independently of each another, represent hydrogen or alkyl.